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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/986,174	11/07/2001	Nabil Hanna	037003-0280732	4956

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EXAMINER	
YU, MISOOK	
ART UNIT	**PAPER NUMBER**
1642	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 09/986,174	**Applicant(s)** HANNA, NABIL	
	Examiner MISOOK YU	**Art Unit** 1642	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 12 June 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *12 June 2007*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): double patenting.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *16 and 23-36*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

MISOOK YU
PRIMARY EXAMINER

MISOOK YU
Primary Examiner
Art Unit: 1642

Continuation of 11. does NOT place the application in condition for allowance because: As for the enablement rejection, applicant argues that the breadth of claims 16 and 29 are both directed to a method comprising administering a therapeutically effective amount of an immunoconjugate to the subject, wherein the immunoconjugate comprises an anti-CD20 antibody or an immunogenic fragment thereof that binds to CD20 expressed by a B cell lymphoma cell in the subject, and wherein said anti-CD20 antibody or immunogenic fragment thereof possesses human effector function, and is fused at its carboxy terminus to interferon-a-2a (IFN-a-2a) that binds a receptor expressed on the surface of an effector cell. At the time the application was filed, it was well-known that anti-CD20 antibodies can be used to kill B cell lymphoma cells and to treat B cell lymphoma. Several known anti- CD20 antibodies are described on page 3, lines 1-12, and the structure of IFN-ct-2a and its role in stimulating cell-killing effector activity by effector cells such as natural killer cells and macrophages was also well known at the time of filing. Applicant argues that the claimed invention is a method for killing B cell lymphoma cells and treating B cell lymphoma in a subject comprising administering a therapeutically effective amount of an immunoconjugate to the subject, wherein the immunoconjugate comprises an anti-CD20 antibody or an immunogenic fragment thereof that binds to CD20 expressed by a B cell lymphoma cell in the subject, and wherein said anti-CD20 antibody or immunogenic fragment thereof possesses human effector function, and is fused at its carboxy terminus to interferon-a-2a (IFN-a-2a) that binds a receptor expressed on the surface of an effector cell. As discussed above, one of skill in the art at the time of filing would have known how to make an anti-CD20 antibody/IFN-a-2a immunoconjugate of the claimed invention, and would also have been able to use known methods for determining a therapeutically effective dosage of a B cell-depleting antibody for treatment of B cell lymphoma. Applicant also argues that with regard to the third factor, the state of the prior art, methods for preparing fusion proteins comprising an antibody conjugated to a cytokine were known at the time of filing, as described on pages 6-7 of the specification. As discussed above, methods for determining a safe and effective dosage of a therapeutic anti-CD20 antibody for the treatment of B cell lymphoma that could be used to determine a therapeutically effective and safe dosage of an anti-CD20 antibody/IFN-a-2a immunoconjugate in order to practice the claimed invention were also known at the time the application was filed. Applicant also argues that skill in the art is high, and the cancer treatment art is relatively predictable, and it would not require an undue experimentation based on amount of guidance provided in the specification.

These arguments have been fully considered but unpersuasive because Davis et al., of record, July 2000, Clinical Cancer Research, vol. 6, pages 2644-2652 represent the state of art using the immunoconjugate of anti-CD20 linked to IFN-alpha-2a. Davis teaches at the abstract that combination therapy with rituximab and IFN-alpha-2a in 38 patients with relapsed or refractory, low-grade or follicular, B-cell NHL was effective, wherein the combination therapy was IFN-alpha-2a [2.5 or 5 million units (MIU)] administered s.c., three times weekly for 12 weeks with the mean total units received were 141 MIU (maximum, 180 MIU). As applicant correctly pointed out during the prosecution history (see page 11 of the Remark's section of the amendment filed on 10/19/2006),= the number of molecules of IFN-alpha-2a being administered is 1,600 fold less than the anti-CD20 antibody in the clinical studies of Davis. The specification does not provide an adequate guidance on the dosage of the immunoconjuate effective to accomplish the purpose stated in the preamble of the claims. Considering the unpredictable state of art, limited guidance, no examples in the specification how to use the instantly claimed invention, broad breath of the claims, it is concluded that undue experimentation is required to practice the invention..

MISOOK YU
PRIMARY EXAMINER